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EXAMINER	
CHANDRA, GYAN	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,753	ARNBERG, HENRIK	
	Examiner	Art Unit	
	GYAN CHANDRA	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-18,21-27 and 29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-18,21-27 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/24/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I (claims 16-29) in the reply filed on 5/28/2008 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, And/Or Claims

The cancellation of claims 19-20 and 28, and the amendments of claims 16, 22, and 27 have been made of record.

Claims 16-18, 21-27 and 29 are pending and under examination.

Information Disclosure Statement

The Information Disclosure Statement (IDS) submitted on 01/24/2007 has been considered.

Claim Objections

Claims 16, 22 and 27 are objected to because of the following informalities:

The Examiner suggests that syntax of claims 16, 22 and 27 can be improved by deleting the word "the" before "GM-CSF" (claim 16, line 5; claim 22, line 1 and claim 27, line 1).

It is noted that because more than one GM-CSF polypeptide is present in the art (also, see claim 29), reciting a GM-CSF along with a sequence identifier would be necessary. Further, GM-CSF has other names such as CSF-2.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-18, 21-27 and 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth a granulocyte-macrophage-colony stimulating factor (GM-CSF), and therefore the written description is not commensurate in scope with “any GM-CSF fragment, or a derivative GM-CSF.”

The claims broadly encompass any GM-CSF fragment; or a derivative of GM-CSF. The claims do not require that a GM-CSF fragment; or a derivative of GM-CSF possess any particular feature or structure that may treat a mammal suffering from a localized bacterial infection or bacterial-related disease. As such a “derivative of GM-CSF or a fragment of GM-CSF” can be a variant, including a mutation, deletion, insertion, or a combination thereof; or any chemical modification of GM-CSF polypeptide or a fragment thereof. Therefore, the instant claims are drawn to a genus of "any GM-CSF fragment, or a derivative of GM-CSF.”

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics

of the genus. Some of the factual considerations that are weighed when determining a written description include the level of skill and knowledge in the art, predictability in the art, the disclosure of complete or partial structures, the disclosure of physical and or chemical properties, adequate disclosure of the functional characteristics, the correlation between structure and function, and disclosure of methods of making.

In the instant case, the specification (on page 8-9) only adequately discloses a GM-CSF polypeptide which when administered in a subject improves periodontitis. The specification does not describe any GM-CSF fragment or any derivative of GM-CSF or any derivative of a GM-CSF fragment that could treat a mammal suffering from any bacterial-related disease. Further, because GM-CSF has many cell differentiation and growth promoting activities; the specification does not disclose how to assign an anti-bacterial activity to a fragment or derivative of GM-CSF. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath Inc. V. Mahurka, 19 USPQ2d 1111, states that applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is *whatever is now claimed* (see page 1117). The specification does

not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (see Vas-Cath at page 1116).

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In Regents of the University of California v. Eli Lilly (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B (1), the court states an adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.

As discussed above, the skilled artisan cannot envision the detailed genus of "any GM-CSF fragment or any derivative of GM-CSF for the treatment of a localized bacterial infection or a bacterial-related disease" and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of making a mutation. The compound itself is required. See Fiers v.Revel, 25USPQ2d 1601 at 1606 (CAFC 1993) and Amgen v.Baird, 30 Chugai

Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 148 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class.

Therefore, only the polypeptide GM-CSF for treating a localized bacterial infection or a bacterial-related disease, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claims 16-18, 21-27 and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a mammal suffering from gingivitis comprising administering therapeutically effective amount of GM-CSF, does not reasonably provide enablement for treating any bacterial-related disease by administering a composition comprising GM-CSF, a fragment or derivative thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to which the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence

or absence of working examples, (6) the breath of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

The instant disclosure fails to meet the enablement requirement for the following reasons:

The instant claims are broadly drawn to a method for treating any localized bacterial infection or any bacterial-related disease in a mammal comprising administering a therapeutically effective amount of at least one GM-CSF polypeptide, fragment or derivative thereof.

The state of the prior art and the predictability or lack thereof in the art:

Grabstein et al. (US Patent No. 5,162,111) teach administering GM-CSF to a subject suffering from a systemic bacterial disease (col. 2, lines 35+). They teach a therapeutic dose for treating bacterial infection in mice (Col. 11, Example 1). Grabstein et al teach that GM-CSF may treat a bacterial infection by promoting macrophage differentiation as well as by promoting immune response against said bacterial infection (col. 4, 35+). Tovey (6,660,258) teaches that the administration of GM-CSF treats a viral infection, allergic disorder, immune system or asthma in a mammal (col.10, lines 15+). Tovey teaches that a number of other cytokines (IL-2, IL-12, IL-15, IL-18, TNF-β) can be used for treating disease that would benefit from TH1 stimulation (col. 21, claim 19). The art teaches treating periodontitis or gingivitis by injecting an antibiotic (Soskolne, Crit. Rev. Oral Biol. Med., Vol. 8: 164-174, 1997). The art does not teach treating a local infection such as periodontitis or gingivitis by administering GM-CSF. The art does not teach administering a fragment of GM-CSF or any derivative of GM-CSF which when administered to a mammal would treat a localized bacterial infection or any bacterial-

related disease. Therefore, it is unpredictable and would require a large amount experimentation to make and use fragments of GM-CSF, derivative of GM-CSF or derivative of GM-CSF fragments as being instantly claimed.

The amount of direction and guidance present and the presence or absence of working examples: Given the teachings found in the art, detailed teachings are required to be present in the disclosure in order to enable the skilled artisan to practice the invention as claimed. These teachings are absent. The specification of pages 8-9 discloses using GM-CSF to treat a patient for periodontitis and gingivitis (Examples 1-2). The specification does not teach that composition comprising GM-CSF when administered locally at the site of infection (e.g., orally for treating a periodontal disease) can treat a bacterial-related disease anywhere in the body, in particular, if the composition is not accessible to said site of infection. Further, the specification does not teach making and using any fragment of GM-CSF or derivative thereof or any derivative of GM-CSF for the treatment of a bacterial-related disease. Because GM-CSF has other cell differentiation and growth promoting activities, it is unpredictable how to make a fragment of derivative of GM-CSF that comprises anti-bacterial activity. The art is devoid of any example where a GM-CSF fragment or derivative thereof; or any derivative of GM-CSF when administered in a mammal treats a localized bacterial infection or bacterial-related disease. Therefore, it is unpredictable how one of the skill in the art can practice the instantly claimed invention.

The breadth of the claims and the quantity of experimentation needed: Due to the large amount of experimentation necessary to make a representative number of GM-

CSF fragments, or derivatives of GM-CSF polypeptide, which could treat a mammal suffering from a localized bacterial infection or any bacterial-related disease, the lack of direction/guidance presented in the specification regarding the same, the state of the prior art which establishes the unpredictability about making and using a representative number of GM-CSF fragments and derivative thereof, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

For the purpose of comparing the prior art with the claimed invention, Claim 16 is being interpreted as a method of treating a mammal suffering from any bacterial disease (the claimed invention is not interpreted as "localized infection").

Claims 16, 21-27 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Grabstein et al (US Patent No. 5,162,111 published on 11/10/1992).

The instant claims are broadly drawn to a method of treating a mammal suffering from a localized bacterial infection or a bacterial-related disease comprising therapeutically effective amount of a composition comprising at least one GM-CSF polypeptide or fragment or derivative thereof having essentially the biological function and activity of GM-CSF, wherein composition is suitable for administration via injection

(claim 21), wherein said GM-CSF or fragment or derivative thereof is present in the composition in a unit dosage amount of 5 µg to 800 µg (claim 22), wherein the unit dosage amount is 50 µg to 100 µg (claim 23), wherein said composition is administered at intervals ranging from once a day to once every third week (claim 24), wherein said composition is administered a total of 1 to 3 times for a period of one week (claim 25), wherein said composition comprises a therapeutically effective amount of at least one other active ingredient (claim 26), and wherein said GM-CSF or fragment or derivative thereof is produced by means of a recombinant expression system (claim 27); and a composition for treating a localized bacterial infection of bacterial-related disease comprising a therapeutically effective amount of a GM-CSF polypeptide or fragment or derivative thereof (claim 29).

Grabstein et al teach a composition comprising GM-CSF for the treatment of bacterial infection (col. 11, lines 50+, Example 1 and claim 1). Grabstein et al teach making GM-CSF using recombinant technology (col. 8, lines 18+, Example 5 and claim 2). They teach that GM-CSF is efficacious as an anti-infective agent (col. 4, lines 35+). They teach administering a recombinant GM-CSF to a subject suffering from bacterial infection in dosages of about 0.05 to 500 ug/Kg of body wt of the subject per day (col. 5, lines18+ and Examples 1-2, and 4) or periodically as contemplated in claim 8, which would be equivalent to 30 µg to 30,000 µg for a 60 Kg subject, and thus the teachings of Grabstein et al meet the limitations of claims 22-26. Grabstein et al teach a composition comprising aqueous solution suitable for intravenous, intramuscular, subcutaneous or peritoneal injection (col. 5, lines 44+ and claims 4-5). They teach administering GM-CSF

in a single or multiple doses (col. 5, line 26). Grabstein et al teach that some variation in dosage will occur depending upon the condition of the subject being treated (col. 5, lines 20+). Therefore, the prior art teaches the instant invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 17 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grabstein et al (US Patent No. 5,162,111) as applied to claims 16, 21-27 and 28 above, and further in view of Sampathkumar (US Patent No. 4,804,530 published on 2/14/1989).

The instant claims are further drawn to a method of treating a mammal suffering from a localized bacterial infection or a bacterial-related disease comprising therapeutically effective amount of a composition comprising at least one GM-CSF

polypeptide or fragment or derivative thereof having essentially the biological function and activity of GM-CSF, wherein the bacterial infection or bacterial-related disease is selected from periodontal disease or sinusitis (claim 17), and wherein the periodontal disease is gingivitis or periodontitis.

The teachings of Grabstein et al are summarized as set forth supra. Grabstein et al do not teach treating a bacterial infection or bacterial related disease selected from periodontal or sinusitis and wherein periodontal disease is gingivitis or periodontitis.

Sampathkumar does teach diseases such as periodontal disease involves bacterial infection (col. 1, lines 27+). Sampathkumar teaches that periodontal diseases affect the periodontum, which is the investing and supporting tissue surrounding a tooth). Sampathkumar teaches that gingivitis and periodontitis are inflammatory disorders of gingiva and the periodontal ligaments, respectively. Sampathkumar teaches that oral cavity diseases which include gingivitis and periodontitis are initiated/and or perpetuated by bacteria in the oral cavity (col. 37+).

Thus, it would have been obvious to one ordinary skilled in the art at the time the instant invention was made to modify the invention of Grabstein who teaches the treatment of bacterial disease using GM-CSF to incorporate the treatment of gingivitis using the GMCSF in view of Sampathkumar who teaches the gingivitis is localized bacterial disease as GM-CSF is known to elicit antibacterial effects. One would have been motivated to do so to because gingivitis is known to be a bacterial disease. One would have a reasonable expectation of success, since the treatment of bacterial

diseases by administering the GM-CSF to a subject has been known in the art at time the instant invention was made.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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